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# Ectopic Pregnancy Among American Indian and Alaska Native Women, 2002–2009

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## **Abstract**

To examine rates of ectopic pregnancy (EP) among American Indian and Alaska Native (AI/AN) women aged 15-44 years seeking care at Indian Health Service (IHS), Tribal, and urban Indian health facilities during 2002-2009. We used 2002-2009 inpatient and outpatient data from the IHS National Patient Information Reporting System to identify EP-associated visits and obtain the number of pregnancies among AI/AN women. Repeat visits for the same EP were determined by calculating the interval between visits; if more than 90 days between visits, the visit was considered related to a new EP. We identified 229,986 pregnancies among AI/AN women 15-44 years receiving care at IHS-affiliated facilities during 2002–2009. Of these, 2,406 (1.05 %) were coded as EPs, corresponding to an average annual rate of 10.5 per 1,000 pregnancies. The EP rate among AI/AN women was lowest in the 15-19 years age group (5.5 EPs per 1,000 pregnancies) and highest among 35–39 year olds (18.7 EPs per 1,000 pregnancies). EP rates varied by geographic region, ranging between 6.9 and 24.4 per 1,000 pregnancies in the Northern Plains East and the East region, respectively. The percentage of ectopic pregnancies found among AI/AN women is within the national 1-2 % range. We found relatively stable annual rates of EP among AI/AN women receiving care at IHS-affiliated facilities during 2002–2009, but considerable variation by age group and geographic region. Coupling timely diagnosis and management with public health interventions focused on tobacco use and sexually transmitted diseases may provide opportunities for reducing EP and EP-associated complications among AI/AN women.

## **Keywords**

Ectopic pregnancy; North American Indians

# **Background**

Ectopic pregnancy (EP) is a potentially life-threatening condition that develops after the implantation of a fertilized ovum outside the endometrial cavity and requires immediate evaluation and treatment [1]. Although studies have found that only 1–2 % of pregnancies in the United States are ectopic and deaths due to EP are decreasing, EP remains an important cause of morbidity and mortality and there are opportunities for prevention [2]. Risk factors for EP include: a history of assisted reproductive technology use; endometriosis; previous obstetrical or gynecological surgery, including tubal sterilization and cesarean section; tubal inflammation and scarring due to infections such as chlamydia and gonorrhea; and disruption of ciliary function attributable to smoking [1, 3–6]. Women affected are not only exposed to complications from the ectopic pregnancy itself and the related treatment procedures, but are also at greater risk of another ectopic pregnancy and infertility [2].

Medical and surgical treatment of ectopic pregnancy is currently provided in both inpatient and outpatient settings in the United States. For this reason, obtaining reliable estimates for the incidence of ectopic pregnancy at the national level and separately for each racial-ethnic group is difficult. The latest such national estimate of 19.7 per 1,000 pregnancies was

reported in 1990–1992 using both inpatient National Hospital Discharge Survey and outpatient National Hospital Ambulatory Medical Care Survey data [5]. More recent attempts to estimate ectopic pregnancy incidence used data from administrative databases [1, 5]. These studies suggest that incidence of ectopic pregnancy has not changed considerably in the United States in the last decade [2].

In 2012, there were about 46,000 live births to American Indian and Alaska Native (AI/AN) women representing 1.2 % of all births in the United States [7]. Yet, little is known about maternal health and pregnancy outcomes among this group of women. Research has shown that AI/AN women have 1.7 times higher rates of severe maternal morbidity than non-Hispanic whites [8], but, to our knowledge, there is no recent population-based estimate of EP incidence among AI/AN women. Nonetheless, compared to non-Hispanic white women, AI/AN women are at higher risk for some of the risk factors for EP, including sexually transmitted diseases (STDs; 9) and smoking before, during, and after pregnancy [10–12]. In addition, AI/AN women have poorer health outcomes in general, and less access to and utilization of health care services [10]. Due to data limitations (e.g. small samples), previous studies have not separately examined EP rates and related risk factors among AI/AN women [1, 13]. Moreover, given that contemporary EP management is frequently provided on an outpatient basis [14], lack of data sources capturing both inpatient and outpatient EP admissions has impeded efforts to ascertain current EP rates in the United States and among AI/AN women separately [5, 13].

The Indian Health Service (IHS), a federal agency within the US Department of Health and Human Services, is responsible for providing health care services to enrolled members of federally-recognized tribes [16]. Every year, IHS and its affiliated Tribal and urban Indian health programs provide health care services to approximately 2.1 million AI/AN through 168 hospitals, health centers, and clinics located in 35 states [17]. IHS data include both inpatient and outpatient visits, thus serving as a representative data source for analysis of a wide range of health outcomes among AI/AN who access care in the IHS/tribal health care system. Both the population and the data source are unique. Not only are pregnancy outcomes among AI/AN women infrequently studied separately from those of other racialethnic groups in the United States, but AI/AN women also appear to be at higher risk of EP and associated complications than other groups of women [18]. Availability of both inpatient and outpatient data in the IHS system provides a unique opportunity to study trends in EP incidence in this sub-population. Notably, there is no comparable data source for all women 15-44 years in the United States. The present analysis examines the rates of and trends in EP among pregnancies of AI/AN women aged 15-44 years seen on an inpatient or outpatient basis within the IHS/tribal health care system during 2002-2009.

# **Methods**

We used direct and contract health service inpatient and outpatient visit data obtained from the IHS National Patient Information Reporting System for the calendar years 2002 through 2009 [19]. These data consist of all hospital discharge and outpatient visit records from IHS, tribally-operated, and IHS-contracted health care facilities that provide healthcare services to

eligible AI/AN [20–22]. For the purpose of this analysis, we used both inpatient and outpatient visits to capture all EP-related visits in the IHS system.

Inpatient and outpatient EP-associated visits were identified using *International* Classification of Diseases, 9th Revision, Clinical Modification (ICD-9-CM) codes 633.x or 761.4 noted on either the inpatient or outpatient visit record [23]. The EP-associated hospitalization and outpatient visits were linked using an IHS-encrypted unique patient identifier to account for women seen as both inpatient and outpatient for the same EPs. Repeat visits for the same EP were determined by calculating the interval between visits; if there were more that 90 days between visits, the visit was considered related to a new EP. The number of pregnancies was determined by selecting hospitalization and outpatient visit records reported with pregnancy listed as one of the diagnoses or procedures (ICD-9-CM diagnosis codes V22, V23, V27, V28, 630-677 or procedure codes 72.0-75.9, 69.01, 69.51, 74.91 or 75.0). Since a woman could have more than one pregnancy during the study period, distinct pregnancies were determined by calculating the interval between visits. If there were nine months or more between visits, the latter visit was counted as related to a new pregnancy. EP-associated rates were expressed as the number of distinct EPs per 1,000 pregnancies among AI/AN women aged 15-44 years. Average annual EP rates between 2000 and 2009 were calculated overall, by 5-year age group, and by geographic region.

IHS has 12 administrative areas: Aberdeen (Iowa, Nebraska, North Dakota, and South Dakota), Alaska (Alaska), Albuquerque (Colorado, New Mexico, and west Texas), Bemidji (Michigan, Minnesota, and Wisconsin), Billings (Montana and Wyoming), California (California), Nashville (all states not belonging to another IHS Area), Navajo (the Navajo Nation), Oklahoma City (Kansas, Oklahoma, most of Texas), Phoenix (all of Arizona except the Tucson and Navajo Areas, Nevada and Utah), Portland (Idaho, Oregon, Washington), Tucson (southern Arizona) [21]. For this analysis, we grouped IHS administrative areas into the following geographic study regions: Alaska (the IHS Alaska Area), East (the IHS Nashville Area), Northern Plains East (the IHS Bemidji Area), Northern Plains West (the IHS Aberdeen and Billings Areas), Southern Plains (the IHS Oklahoma City Area), Southwest (the IHS Albuquerque, Navajo, Phoenix, and Tucson Areas), and West (the IHS California and Portland Areas).

Because age- and region-specific annual rates based on small numbers (fewer than 20 EPs) are considered unreliable, and some cells in our study had fewer than 20 EPs, we calculated 3-year moving averages to smooth the data and gain stability over time with a minimal loss of information [24]. We conducted the trend analysis over the study period using Poisson regression, controlling for over-dispersion [25]. Comparisons of EP-associated rates between groups were made using Poisson regression analysis to determine rate ratios (RRs) and 95 % confidence intervals (CIs). Statistical tests were considered significant at p < 0.05 level. Since patients are not individually identifiable per HHS Office for Human Research Protections guidance, this analysis was deemed exempt from review by Centers for Disease Control and Prevention's Institutional Review Board.

## Results

We identified a total of 229,986 pregnancies to AI/AN women aged 15–44 years during 2002–2009. Of these, 2,406 (1.05 %) were coded as EPs, corresponding to an average annual rate of 10.5 EPs per 1,000 pregnancies. Recurring EP occurred in 6.1 % (N = 138) of women. Of these, nine women had three EPs and two women had four EPs during 2002–2009. Of the AI/AN women who experienced an EP, 71.0 % were seen only as outpatients, 9.8 % were seen only as inpatients, and 19.3 % were seen as both outpatients and inpatients for the same EP.

The average annual EP rate among AI/AN women was lowest among women aged 15–19 years (5.5 per 1,000 pregnancies) and highest among those aged 35–39 years (18.7 EPs per 1,000 pregnancies; Table 1). Compared to AI/AN women aged 15–19 years, women aged 35–39 years were 3.4 times more likely to have an EP (95 % CI 2.90–4.03; p <.001). The average annual EP rates were stable for most age groups throughout the study period, without significant year-to-year variations (Fig. 1).

The average annual EP rates varied considerably by geographic region. The lowest EP rates were seen in the Northern Plains East region (2000–2009 average of 6.9 EPs per 1,000 pregnancies) and the highest rates were seen in the East region (2000–2009 average of 24.4 EPs per 1,000 pregnancies). Compared with EP rates in the Northern Plains East region, rates in the East region were 3.6 times greater (95 % CI 2.75–4.57; p <.001) (Table 1). EP rates were stable for most regions throughout the study period. Trends in only two regions were statistically significantly different over time: EP rates in the West region increased, while those in the Southern Plains region decreased (Fig. 2).

## **Discussion**

We analyzed IHS inpatient and outpatient visit data for AI/AN women aged 15–44 years and described EP rates and trends during 2002–2009. We found stable rates of EP overall with considerable variation by age and region. The 2002–2009 average annual EP rate in our study (10.5 EPs per 1,000 pregnancies) was higher than the EP incidence rate reported by Hoover et al. [1] for the entire US population (6.4 EPs per 1,000 pregnancies), but far less than the rate reported by Trabert et al. [13] for women belonging to the Group Health Cooperative, a large health management organization (24.5 EPs per 1,000 pregnancies). The latter study included 2,114 women between the ages of 15–44 years living in Washington State and western Idaho who sought services through the integrated group practice portion of the health care cooperative; the extent to which risk behaviors and access to health care differ between their study population and ours is unknown.

Several previous studies have demonstrated considerable variation in EP rates by geographic region. One such study looked at 2002–2003 EP rates in the Medicaid population in California, Illinois, and New York by race/ethnicity. As in our study, EP rates varied by geographic location [26]. In California's Medicaid population, the overall EP rate was 20.7 per 1,000 pregnancies and the AI/AN rate was 12.1 per 1,000 pregnancies. In Illinois' Medicaid population, the overall EP rate was 24.3 per 1,000 pregnancies and the AI/AN rate

was 31.1 per 1,000 pregnancies. In New York's Medicaid population, the EP rate was 23.8 per 1,000 pregnancies and the AI/AN rate was 12.1 per 1,000 pregnancies [26]. AI/AN EP rates reported for California's and New York's Medicaid populations are in line with our study's average rate of 12.2 per 1,000 pregnancies. Notably, rates among AI/AN women in all three states were only lower than the corresponding rates in non-Hispanic black women, which ranged between 25.5 and 35.1 EPs per 1,000 pregnancies in New York and Illinois, respectively; EP rates among non-Hispanic white women ranged between 22.6 and 24.5 per 1,000 pregnancies in New York and Illinois, respectively. Not surprisingly, regional differences among AI/AN women have been found in relation to other health outcomes. For example, invasive cervical cancer incidence rates vary nearly twofold across IHS regions, with the highest rates reported in the Southern and Northern Plains regions and the lowest rate in the Eastern region and the Pacific Coast region [27]. Our study finds the highest rate of EP in the Eastern region and the lowest rate in the Northern Plains region; moreover, the corresponding EP rate ratio is considerably greater than the invasive cervical cancer rate ratio between the regions with highest and lowest rates of invasive cervical cancer. Taken together, these findings indicate an important need for all AI/AN women's health services to include both reproductive health screenings and education on pregnancy complications, including ectopic pregnancy.

Several behavioral risks have been linked to EP, including smoking and STDs [1, 3–6]. Disruption of ciliary function related to smoking is a reported risk factor for EP [6]. National behavioral surveillance data have shown AI/AN women to be at higher risk than white non-Hispanic women for smoking before, during, and after pregnancy [10–12]. While many IHS, Tribal, and urban health care providers may regularly screen patients for tobacco use and offer smoking cessation interventions, IHS's current reported rate of this practice (35.2 %) is well below the Healthy People 2020 goal of 80 % [28–30]. There is need to identify key opportunities to expand tobacco screening and cessation interventions among AI/AN women of childbearing age, including at federally-funded Women, Infants, and Children clinics.

Throughout the United States, there is considerable geographic variation in STD rates between racial/ethnic groups [9]; AI/AN women have the second highest rates of chlamydia and gonorrhea in the country by race/ethnicity. This disparity is even more pronounced among women in older age groups (30–34, 35–39, 40–44 years), where chlamydia and gonorrhea rates among AI/AN women are 4.6 to 5.9 times higher than among white non-Hispanic women [9]. Several regions in our analysis, especially Alaska and Northern Plains West regions, have both high EP rates and high STD rates among AI/AN women [9]. It is possible that some variations in EP rates may be related to increases in STD screening and treatment. However, such an association is difficult to confirm. Still, early STD detection may reduce tubal damage by accurate and prompt detection and treatment of lower genital tract infections [31, 32]. While screening for STDs is common practice in IHS facilities, and especially so among women of reproductive age, coverage and adherence to nationally recommended screening guidelines can be further improved [31–34].

Our study has some limitations. The EP rates may be underestimated, as case ascertainment was based on IHS administrative data and ICD-9-CM codes. While the majority of these data (96 %) were submitted via the IHS's Resource and Patient Management System, some

tribal and urban sites submit data using other data management systems. Diagnoses may be incomplete or inaccurate due to use of ICD-9-CM coding to identify EP visits. We also may have underestimated the number of EPs and pregnancies, as some AI/AN women who normally receive services in the IHS/tribal health system may have accessed obstetric and emergency services from outside sources. Therefore, our findings are not generalizable to the AI/AN population who do not access care through the IHS system. The total number of pregnancies used in our rate calculations may be underestimated, since information on miscarriages and abortions is often incomplete. By defining a single pregnancy as a 9-month period, we may have introduced bias and underestimated pregnancies by systematically excluding short pregnancy intervals. In the data available to us, we could not differentiate the type of treatment obtained by women accessing EP care through IHS; it would have been especially important to differentiate between types of treatment obtained in the outpatient settings. Lastly, the reasons behind the geographical variation in EP rates remain unknown.

To our knowledge, this study is the first to provide EP-associated rates among AI/AN women of reproductive age. Overall, only a few, and by and large, older published studies have described EP rates by racial/ethnic groups, and even fewer included EP data for AI/AN women [26, 35–39]. As with other studies examining EPs [13–15, 40], the majority of women with an EP in our study received care in an outpatient setting only. We recommend analyzing visits from both inpatient and outpatient settings when conducting EP surveillance and/or research to identify the greatest number of EPs.

This study highlights the need for further investigation of the relationship between elevated rates of smoking and STDs among AI/AN women and EP rates. Efforts to reduce EP rates among AI/AN women should include heightened public awareness of the need for regular and routine well-woman exams in order to diagnose and treat EP promptly and to address known risk factors for EP, including tobacco use. Improved adherence to national STD screening guidelines, prompt treatment of STDs, and tobacco screening and cessation interventions may potentially lead to a decline in EP incidence [1, 4, 6].

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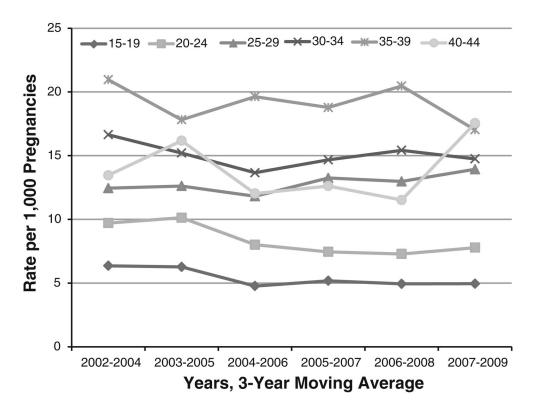
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**Fig. 1.**Ectopic pregnancy rates among American Indian and Alaska Native women by age group and time period: United States, 2002–2009. A Poisson Regression Trend Test of 3-year moving averages controlling for over-dispersion was conducted; no significant trends detected

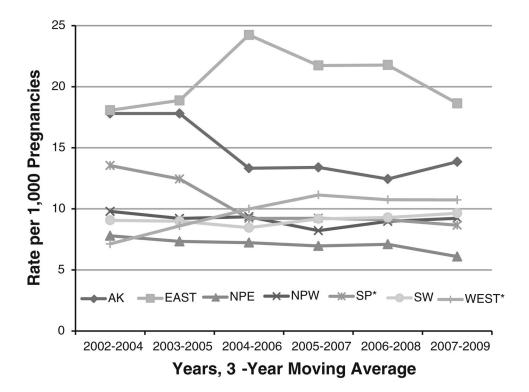


Fig. 2.

Ectopic pregnancy rates among American Indian and Alaska Native women by region and time period: United States, 2002–2009. Regions are Alaska (AK; the IHS Alaska Area), East (the IHS Nashville Area), Northern Plains East (NPE; the IHS Bemidji Area), Northern Plains West (NPW; the IHS Aberdeen and Billings Areas), Southern Plains (SP; the IHS Oklahoma City Area), Southwest (SW; the IHS Albuquerque, Navajo, Phoenix, and Tucson Areas), and West (the IHS California and Portland Areas). A Poisson Regression Trend Test of 3-year moving averages controlling for over-dispersion was conducted; no significant trends detected. Only trends in the Southern Plains and West regions were statistically significant (indicated with *asterisk*)

Table 1

Ectopic pregnancy rates among American Indian and Alaska native women age 15–44 years, by age group and region, 2002–2009, United States

	Average annual rate per 1,000 population <sup>a</sup>	Rate ratio (95 % confidence interval)	p value
Age (years)			
15–19	5.5	_b	_
20–24	8.5	1.56 (1.36–1.79)	< 0.0001
25–29	13.0	2.38 (2.07–2.73)	< 0.0001
30–34	15.0	2.75 (2.37–3.19)	< 0.0001
35–39	18.7	3.42 (2.90–4.03)	< 0.0001
40–44	14.3	2.62 (2.02–3.36)	< 0.0001
Region			
Northern Plains East	6.9	_b	_
Alaska	14.9	2.17 (1.73–2.72)	< 0.0001
East	24.4	3.55 (2.75–4.57)	< 0.0001
Northern Plains West	9.4	1.36 (1.08–1.71)	0.0084
Southern Plains	10.7	1.56 (1.25–1.95)	< 0.0001
Southwest	9.2	1.33 (1.07–1.65)	0.0088
West	9.5	1.39 (1.09–1.77)	0.0082

Regions are Alaska (the IHS Alaska Area), East (the IHS Nashville Area), Northern Plains East (the IHS Bemidji Area), Northern Plains West (the IHS Aberdeen and Billings Areas), Southern Plains (the IHS Oklahoma City Area), Southwest (the IHS Albuquerque, Navajo, Phoenix, and Tucson Areas), and West (the IHS California and Portland Areas)

 $<sup>^</sup>a$ The denominator was the number of pregnancies among AI/AN women 15–44 years old seen in IHS facilities during 2002–2009

<sup>&</sup>lt;sup>b</sup>Referent category